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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/014,220

11/09/2001

Che-Kun James Shen

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20872 7590 12/20/2006  
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EXAMINER

KAUSHAL, SUMESH

ART UNIT

PAPER NUMBER

1633

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

12/20/2006

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

# Office Action Summary

Application No.

10/014,220

Applicant(s)

SHEN, CHE-KUN JAMES

Examiner

Sumesh Kaushal Ph.D.

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 27 September 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 21-34 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Applicant's response and Dr. Shen's declaration filed on 09/27/06 has been acknowledged.

*Claims 21-34 are pending and are examined in this office action.*

*Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300.*

*The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.*

### ***Claim Rejections - 35 USC § 112***

Claims 21-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the same reasons of record as set forth in the office action mailed on 06/27/06.

In response filed on 09/27/06 the applicant amended the base claim 21 to recite claim new limitation "integrated". There is no support such claim limitation the speciation as filed. As MPEP 2163.06 notes " If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981). So instant claims encompasses apparently a new matter. No pages or place in the specification was cited to support this amendment. A careful review by the examiner of the specification failed to identify any support for this new limitation. Since no basis has been found to support the new claim limitation in the specification, the claims are rejected as incorporating new matter.

### **Response to arguments**

The applicant arguments regarding new matter issue on pages 4-5 of response filed on 09/27/06 has been fully considered. The applicant argues that the subject matter of claims need not to be described literally in order for disclosure to satisfy the written description requirement. The applicant argues that support for the limitation "intergrated" may also be found in the specification which states "[0004] Gene expression in transgenic animals is often limited by the position in the genome where the transgene is integrated and by the number of copies of the transgene which have been integrated."

However, applicant's arguments are found not persuasive. MPEP clearly states that whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). In the instant case the specification fails to support the claim limitation which encompasses genomic DNA comprising at least one copy of integrated transgene (as claimed). The para [004] in the specification is merely reflect a generic state of the transgenic art and does not describe that the transgene as claimed herein is infect integrated in the genomic DNA. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)).

As stated earlier the specification as filed fails to disclose that the transgene (as claimed) is in an integrated form especially in context of an isolated animal cells.

***Claim Rejections - 35 USC § 102/103***

Claims 21, 23-27 and 30-32 stand rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Zhang et al (JBC 270(15):8501-8505, 1995, *ref of record on PTO 1449*) in view of Ohtani et al, Nucleic Acids Res. 25;17(4):1589-604, 1989, for the same reasons of record as set forth in the office action mailed on 06/27/06.

**Response to arguments and Dr. Shen's declaration**

The applicant arguments regarding prior art anticipation issue on pages 5-6 of response filed on 09/27/06 has been fully considered. The applicant argues that Ohtani et al don not support the assertion that after only five days of culturing as taught by Zhang was sufficient for stable integration into the genome. The applicant argues Ohtani et al. only observed stably transfected cells after fourteen days, not after five days. Furthermore, as indicated in the declaration of Dr, Shen provided with this response, even after five days, the vector would not have integrated into the genome. The applicant argues that Ohtani et al. and the papers that it cites teach the integration efficiency when conditions are optimized to achieve integration. The applicant argues that the plasmid that Zhang et al. used was not a linear plasmid but rather was a circularized plasmid, which would have reduced the frequency of integration. The applicant argues that office fails to demonstrate that that the circularized vector necessarily would have integrated within the five-day period and applicants have submitted a declaration stating that it would not have integrated within the five-day period (also see declaration filed 9/27/06).

However, applicant's arguments are found not persuasive because given the broadest reasonable interpretation all what is required to anticipate the invention as claimed is single cell whose genomic DNA comprises alt least one copy of an integrated

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transgene (as claimed). The office has provided a clear evidence that Zhang et al clearly teaches electroporation of at least  $10^7$  cells which after transfection would had contained at least 50 stably transfected cells according to Ohtani or at least  $10^3$ - $10^5$  according to applicant own assertion that only one every  $10^2$ - $10^4$  cells is transfected. Thus the cited art clearly established that electroporation results in stable transfection of foreign genes into human host cells. In addition, the cited art teaches the use of selectable makers for the isolation of homogeneous cell population that express stably transfected gene, which inherently establishes that the cells were transfected a the time of electroporation (day=0) which would had survived any length of time under any culture conditions (i.e. day 5-14, or more). Thus given the broadest reasonable interpretation the cited art clearly anticipate the invention as claimed which inherently teaches isolated animal cells having chromosomal integration of the transgene. Thus given the broadest reasonable interpretation the cited art clearly anticipate the invention as claimed.

Claims 22, 28-29 and 33-34 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al (JBC 270(15):8501-8505, 1995, *ref of record on PTO 1449*) as applied to claims 21-27 and 30-32 above, and further in view of Zhang et al (Mol Cell Biol. 4:2298-308, 1993, *ref of record on PTO 1449*) , for the same reasons of record as set forth in the office action mailed on 06/27/06.

#### **Response to arguments and Dr. Shen's declaration**

The applicant argues that invention as claimed is not prima facie obvious in view of prior art of record as the obviousness may be rebutted by showing superior or unexpected results. The applicant argues that the TCTGAGTCA sequence when used in chromosomally integrated expression construct shows superior and unexpected results. The applicant argues that the specification in Table I show that when the mutant HS-40 transgene is used a strong positive correlation between copy number of the transgene and hGH expression is observed. The fact that the wild-type HS-40 element does not provide such position independent expression proves that one of skill in the art would not expect that the presently claimed mutant HS-40 element would provide this

result. The applicant argues that Dr. Shen declaration further supports the assertion that this result is an unexpected finding.

The applicant argues that the office has asserted that it would not be unexpected that the mutant HS-40 element provides position independent expression. The applicant argues that the specification clearly indicates that the wild-type HS-40 does not provide position independent expression as is claimed; so one of skill in the art could not expect that the mutant HS-40 as claimed provides position independent expression. The applicant argues that it is irrelevant that other elements exist that provides position independent expression. The applicant argues that the position independent expression provided by the claimed invention is unexpected, and the article Waltccs et al., PNAS 92:7125-7129, 1993) simply does not support the examiner's assertion that enhancers generally provide position independent expression.

However, applicant's arguments are found not persuasive because invention as claimed is not limited to any position independent expression as asserted by the applicant. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., position independent expression) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case Zhang (1995) clearly teaches the evaluation of transgene activity after electroporation which is sufficient enough to evaluate any position independent expression. In addition position independent activity of the enhancer as claimed is not an unexpected property because it has been well known in the art that presence of an enhancer in a transgene

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tends to provide position independent expression (see Walters et al, PNAS 92:7125-7129, 1995). In addition, the position independent expression is not an unexpected finding, since the cited art clearly teaches that HS-40 enhancer element is capable of expressing in variety of cells types i.e. K562, MEL and HeLa cells. Thus the invention as claimed is prima facie obvious in view of cited prior art of record.

### ***Conclusion***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should



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you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547**. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**



**SUMESH KAUSHAL  
PRIMARY EXAMINER  
ART UNIT 1633**